HPV 45 L1 Nucleotide Sequence Alignment

45 L1 wt	(1)	ATGGCTTTGTGGCGGCCTAGTGACAGTACGGTATATCTTCCACCACCTTC
45 L1 R	(1)	............A.A..ATC....TC...T..C..CT.G........A..
45 L1 wt	(51)	TGTGGCCAGAGTTGTCAACACTGATGATTATGTGTCTCGCACAAGCATAT
45 L1 R	(51)	...C..T.....C...........C..C..C..C..CA.A..CTC...C.
45 L1 wt	(101)	TTTACCATGCAGGCAGTTCCCGATTATTAACTGTAGGCAATCCATATTTT
45 L1 R	(101)	.C.....C..T..TTC....A....G..G.....C..T..C.....C..C
45 L1 wt	(151)	AGGGTTGTACCTAGTGGTGCAGGTAATAAACAGGCTGTTCCTAAGGTATC
45 L1 R	(151)	..A..C..C..ATCC.....T.....C..G..A........A.....C..
45 L1 wt	(201)	CGCATATCAGTATAGGGTGTTTAGAGTAGCTTTGCCCGATCCTAATAAAT
45 L1 R	(201)	T..T..C..A..C..A..C..C.....C........A..C..A..C..G.
45 L1 wt	(251)	TTGGATTACCTGATTCTACTATATATAATCCTGAAACACAACGTTTGGTT
45 L1 R	(251)	.C..T..G..A..C........C..C..C..A.....T...A.A.....C
45 L1 wt	(301)	TGGGCATGTGTAGGTATGGAAATTGGTCGTGGGCAGCCTTTAGGTATTGG
45 L1 R	(301)	........C..C...........C...A.A..T..A..A..G.....C..
45 L1 wt	(351)	CCTAAGTGGCCATCCATTTTATAATAAATTGGATGATACAGAAAGTGCTC
45 L1 R	(351)	TT.GTC...T..C.....C..C..C..G.....C..C..C...TCC....
45 L1 wt	(401)	ATGCAGCTACAGCTGTTATTACGCAGGATGTTAGGGATAATGTGTCAGTT
45 L1 R	(401)	.C..T.....T.....C..C..T..A..C..C..A..C..C..C..T..C
45 L1 wt	(451)	GATTATAAGCAAACACAGCTGTGTATTTTAGGTTGTGTACCTGCTATTGG
45 L1 R	(451)	..C..C........C..AT.......C..G........C..A.....C..
45 L1 wt	(501)	TGAGCACTGGGCCAAGGGCACACTTTGTAAACCTGCACAATTGCAACCTG
45 L1 R	(501)	...A........T.....T..CT.G.....G..A..T...........A.
45 L1 wt	(551)	GTGACTGTCCTCCTTTGGAACTTAAAAACACCATTATTGAGGATGGTGAT
45 L1 R	(551)	..........A..A......T.G..G.....T..C..C..A..C.....C

FIG.1A

```
45 L1 wt   ( 601)   ATGGTGGATACAGGTTATGGGGCAATGGATTTTAGTACATTGCAGGATAC
45 L1 R    ( 601)   .....T..C..T.....C..T..T.....C..CTCC..CC.......C..

45 L1 wt   ( 651)   AAAGTGCGAGGTTCCATTAGACATTTGTCAATCCATCTGTAAATATCCAG
45 L1 R    ( 651)   T.....T..A........G.....C........T........G..C....

45 L1 wt   ( 701)   ATTATTTGCAAATGTCTGCTGATCCCTATGGGGATTCTATGTTTTTTTGC
45 L1 R    ( 701)   .C..C...........C.....C..A..C..T..C........C..C..T

45 L1 wt   ( 751)   CTACGCCGTGAACAACTGTTTGCAAGACATTTTTGGAATAGGGCAGGTGT
45 L1 R    ( 751)   T.GA.AA.A......T....C..T.....C..C.....C..A..T.....

45 L1 wt   ( 801)   TATGGGTGACACAGTACCTACAGACCTATATATTAAAGGCACTAGCGCTA
45 L1 R    ( 801)   C...........T..T..A..T...T.G..C..C..G..T..CTCT....

45 L1 wt   ( 851)   ATATGCGTGAAACCCCTGGCAGTTGTGTGTATTCCCCTTCTCCCAGTGGC
45 L1 R    ( 851)   .C...A.A.....T..A..TTCC.....C..C..T..A.....ATC...T

45 L1 wt   ( 901)   TCTATTACTACTTCTGATTCTCAATTATTTAATAAGCCATATTGGTTACA
45 L1 R    ( 901)   .....C........C..C........G..C..C........C.....G..

45 L1 wt   ( 951)   TAAGGCCCAGGGCCATAACAATGGTATTTGTTGGCATAATCAGTTGTTTG
45 L1 R    ( 951)   C.....T..A..T..C.....C.....C........C..C..A.....C.

45 L1 wt   (1001)   TTACTGTAGTGGACACTACCCGCAGTACTAATTTAACATTATGTGCCTCT
45 L1 R    (1001)   .C..C..C..T.........A.ATC......C..G..C..G.....T...

45 L1 wt   (1051)   ACACAAAATCCTGTGCCAAATACATATGATCCTACTAAGTTTAAGCACTA
45 L1 R    (1051)   ..T.....C..A..T.....C..T..C..C..A..C.....C........

45 L1 wt   (1101)   TAGTAGACATGTGGAGGAATATGATTTACAGTTTATTTTTCAGTTGTGCA
45 L1 R    (1101)   CTCC.....C..C........C..C..G..A..C..C..C..A.....T.

45 L1 wt   (1151)   CTATTACTTTAACTGCAGAGGTTATGTCATATATCCATAGTATGAATAGT
45 L1 R    (1151)   ....C..C..G..C..T..A..C.....C..C..T..CTC......CTCC

45 L1 wt   (1201)   AGTATATTGGAAAATTGGAATTTTGGTGTACCTCCACCACCTACTACAAG
45 L1 R    (1201)   TC...C........C.....C..C.....T..A........A..C..CTC
```

FIG.1B

```
45 L1 wt    (1251)  TTTAGTGGATACATATCGTTTTGTGCAATCAGTTGCTGTTACCTGTCAAA
45 L1 R     (1251)  C..G..T..C..T..CA.A..C..C.....T..C.....C..T.......

45 L1 wt    (1301)  AGGATACTACACCTCCAGAAAAGCAGGATCCATATGATAAATTAAAGTTT
45 L1 R     (1301)  ....C..C..T..A...........A..C.....C..C..G..G.....C

45 L1 wt    (1351)  TGGACTGTTGACCTAAAGGAAAAATTTTCCTCCGATTTGGATCAATATCC
45 L1 R     (1351)  ............T.G........G..C..T.....C.....C.....C..

45 L1 wt    (1401)  CCTTGGTCGAAAGTTTTTAGTTCAGGCTGGGTTACGTCGTAGGCCTACCA
45 L1 R     (1401)  AT.G...A.......C..G.....A.....T..GA.A.....A..A..T.

45 L1 wt    (1451)  TAGGACCTCGTAAGCGTCCTGCTGCTTCCACGTCTACTGCATCTAGGCCT
45 L1 R     (1451)  .C..T..A......A.A..A...........T..C.....T.....A..A

45 L1 wt    (1501)  GCCAAACGTGTACGTATACGTAGTAAAAAATAA (SEQ ID NO:3)
45 L1 R     (1501)  ..T..G.....CA.A..CA.ATCC..G..G...(SEQ ID NO:1)
```

FIG.1C

Synthetic HPV 45 L1 Nucleotide and Amino Acid Sequences

```
     M  A  L  W   R  P  S   D  S  T   V  Y  L  P   P  P  S
1    ATGGCTTTGT GGAGACCATC TGACTCTACT GTCTACTTGC CACCACCATC
     TACCGAAACA CCTCTGGTAG ACTGAGATGA CAGATGAACG GTGGTGGTAG
      V  A  R   V  V  N  T   D  D  Y   V  S  R   T  S  I  F
51   TGTCGCTAGA GTCGTCAACA CTGACGACTA CGTCTCCAGA ACCTCCATCT
     ACAGCGATCT CAGCAGTTGT GACTGCTGAT GCAGAGGTCT TGGAGGTAGA
      Y  H  A   G  S  S   R  L  L  T   V  G  N   P  Y  F
101  TCTACCACGC TGGTTCTTCC AGATTGTTGA CTGTCGGTAA CCCATACTTC
     AGATGGTGCG ACCAAGAAGG TCTAACAACT GACAGCCATT GGGTATGAAG
     R  V  V  P   S  G  A   G  N  K   Q  A  V  P   K  V  S
151  AGAGTCGTCC CATCCGGTGC TGGTAACAAG CAAGCTGTTC CAAAGGTCTC
     TCTCAGCAGG GTAGGCCACG ACCATTGTTC GTTCGACAAG GTTTCCAGAG
      A  Y  Q   Y  R  V  F   R  V  A   L  P  D   P  N  K  F
201  TGCTTACCAA TACAGAGTCT TCAGAGTCGC TTTGCCAGAC CCAAACAAGT
     ACGAATGGTT ATGTCTCAGA AGTCTCAGCG AAACGGTCTG GGTTTGTTCA
      G  L  P   D  S  T   I  Y  N  P   E  T  Q   R  L  V
251  TCGGTTTGCC AGACTCTACT ATCTACAACC CAGAAACTCA AAGATTGGTC
     AGCCAAACGG TCTGAGATGA TAGATGTTGG GTCTTTGAGT TTCTAACCAG
     W  A  C  V   G  M  E   I  G  R   G  Q  P  L   G  I  G
301  TGGGCATGCG TCGGTATGGA AATCGGTAGA GGTCAACCAT TGGGTATCGG
     ACCCGTACGC AGCCATACCT TTAGCCATCT CCAGTTGGTA ACCCATAGCC
      L  S  G   H  P  F  Y   N  K  L   D  D  T   E  S  A  H
351  TTTGTCTGGT CACCCATTCT ACAACAAGTT GGACGACACC GAATCCGCTC
     AAACAGACCA GTGGGTAAGA TGTTGTTCAA CCTGCTGTGG CTTAGGCGAG
      A  A  T   A  V  I   T  Q  D  V   R  D  N   V  S  V
401  ACGCTGCTAC TGCTGTCATC ACTCAAGACG TCAGAGACAA CGTCTCTGTC
     TGCGACGATG ACGACAGTAG TGAGTTCTGC AGTCTCTGTT GCAGAGACAG
     D  Y  K  Q   T  Q  L   C  I  L   G  C  V  P   A  I  G
451  GACTACAAGC AAACCCAATT GTGTATCTTG GGTTGTGTCC CAGCTATCGG
     CTGATGTTCG TTTGGGTTAA CACATAGAAC CCAACACAGG GTCGATAGCC
      E  H  W   A  K  G  T   L  C  K   P  A  Q   L  Q  P  G
501  TGAACACTGG GCTAAGGGTA CCTTGTGTAA GCCAGCTCAA TTGCAACCAG
     ACTTGTGACC CGATTCCCAT GGAACACATT CGGTCGAGTT AACGTTGGTC
```

FIG.2A

D C P P L E L K N T I I E D G D
551 GTGACTGTCC ACCATTGGAA TTGAAGAACA CTATCATCGA AGACGGTGAC
CACTGACAGG TGGTAACCTT AACTTCTTGT GATAGTAGCT TCTGCCACTG
M V D T G Y G A M D F S T L Q D T
601 ATGGTTGACA CTGGTTACGG TGCTATGGAC TTCTCCACCC TGCAGGACAC
TACCAACTGT GACCAATGCC ACGATACCTG AAGAGGTGGG ACGTCCTGTG
K C E V P L D I C Q S I C K Y P D
651 TAAGTGTGAA GTTCCATTGG ACATCTGTCA ATCTATCTGT AAGTACCCAG
ATTCACACTT CAAGGTAACC TGTAGACAGT TAGATAGACA TTCATGGGTC
Y L Q M S A D P Y G D S M F F C
701 ACTACTTGCA AATGTCCGCT GACCCATACG GTGACTCTAT GTTCTTCTGT
TGATGAACGT TTACAGGCGA CTGGGTATGC CACTGAGATA CAAGAAGACA
L R R E Q L F A R H F W N R A G V
751 TTGAGAAGAG AACAATTGTT CGCTAGACAC TTCTGGAACA GAGCTGGTGT
AACTCTTCTC TTGTTAACAA GCGATCTGTG AAGACCTTGT CTCGACCACA
M G D T V P T D L Y I K G T S A N
801 CATGGGTGAC ACTGTTCCAA CTGACTTGTA CATCAAGGGT ACCTCTGCTA
GTACCCACTG TGACAAGGTT GACTGAACAT GTAGTTCCCA TGGAGACGAT
M R E T P G S C V Y S P S P S G
851 ACATGAGAGA AACTCCAGGT TCCTGTGTCT ACTCTCCATC TCCATCTGGT
TGTACTCTCT TTGAGGTCCA AGGACACAGA TGAGAGGTAG AGGTAGACCA
S I T T S D S Q L F N K P Y W L H
901 TCTATCACTA CTTCCGACTC TCAATTGTTC AACAAGCCAT ACTGGTTGCA
AGATAGTGAT GAAGGCTGAG AGTTAACAAG TTGTTCGGTA TGACCAACGT
K A Q G H N N G I C W H N Q L F V
951 CAAGGCTCAA GGTCACAACA ACGGTATCTG TTGGCACAAC CAATTGTTCG
GTTCCGAGTT CCAGTGTTGT TGCCATAGAC AACCGTGTTG GTTAACAAGC
T V V D T T R S T N L T L C A S
1001 TCACCGTCGT TGACACTACC AGATCTACTA ACTTGACCTT GTGTGCTTCT
AGTGGCAGCA ACTGTGATGG TCTAGATGAT TGAACTGGAA CACACGAAGA
T Q N P V P N T Y D P T K F K H Y
1051 ACTCAAAACC CAGTTCCAAA CACTTACGAC CCAACCAAGT TCAAGCACTA
TGAGTTTTGG GTCAAGGTTT GTGAATGCTG GGTTGGTTCA AGTTCGTGAT
S R H V E E Y D L Q F I F Q L C T
1101 CTCCAGACAC GTCGAGGAAT ACGACTTGCA ATTCATCTTC CAATTGTGTA
GAGGTCTGTG CAGCTCCTTA TGCTGAACGT TAAGTAGAAG GTTAACACAT
I T L T A E V M S Y I H S M N S
1151 CTATCACCTT GACCGCTGAA GTCATGTCCT ACATTCACTC TATGAACTCC
GATAGTGGAA CTGGCGACTT CAGTACAGGA TGTAAGTGAG ATACTTGAGG

FIG.2B

```
        S  I  L  E   N  W  N   F  G  V   P  P  P  P   T  T  S
1201    TCTATCTTGG AAAACTGGAA CTTCGGTGTT CCACCACCAC CAACCACCTC
        AGATAGAACC TTTTGACCTT GAAGCCACAA GGTGGTGGTG GTTGGTGGAG
         L  V  D   T  Y  R  F   V  Q  S   V  A  V   T  C  Q  K
1251    CTTGGTTGAC ACTTACAGAT TCGTCCAATC TGTCGCTGTC ACTTGTCAAA
        GAACCAACTG TGAATGTCTA AGCAGGTTAG ACAGCGACAG TGAACAGTTT
         D  T  T   P  P  E   K  Q  D  P   Y  D  K   L  K  F
1301    AGGACACCAC TCCACCAGAA AAGCAAGACC CATACGACAA GTTGAAGTTC
        TCCTGTGGTG AGGTGGTCTT TTCGTTCTGG GTATGCTGTT CAACTTCAAG
        W  T  V  D   L  K  E   K  F  S   S  D  L  D   Q  Y  P
1351    TGGACTGTTG ACTTGAAGGA AAAGTTCTCT TCCGACTTGG ACCAATACCC
        ACCTGACAAC TGAACTTCCT TTTCAAGAGA AGGCTGAACC TGGTTATGGG
         L  G  R   K  F  L  V   Q  A  G   L  R  R   R  P  T  I
1401    ATTGGGTAGA AAGTTCTTGG TTCAAGCTGG TTTGAGACGT AGACCAACTA
        TAACCCATCT TTCAAGAACC AAGTTCGACC AAACTCTGCA TCTGGTTGAT
          G  P  R   K  R  P   A  A  S  T   S  T  A   S  R  P
1451    TCGGTCCACG TAAGAGACCA GCTGCTTCCA CTTCCACTGC TTCTAGACCA
        AGCCAGGTGC ATTCTCTGGT CGACGAAGGT GAAGGTGACG AAGATCTGGT
        A  K  R  V   R  I  R   S  K  K   * (SEQ ID NO:2)
1501    GCTAAGCGTG TCAGAATCAG ATCCAAGAAG TAA (SEQ ID NO:1)
        CGATTCGCAC AGTCTTAGTC TAGGTTCTTC ATT (SEQ ID NO:8)
```

FIG.2C

NORTHERN BLOT ANALYSIS OF HPV 45 L1 R.

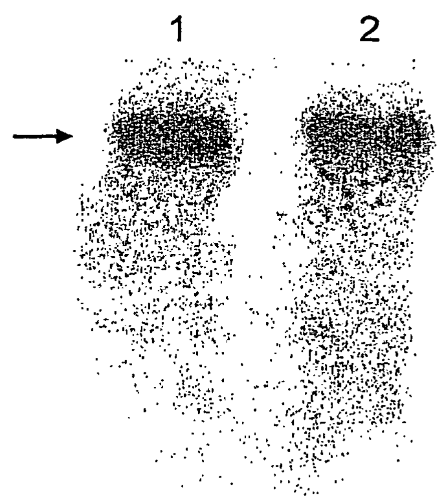

FIG.3

WESTERN BLOT OF HPV 45 L1 wt AND
HPV 45 L1 R ISOLATES.

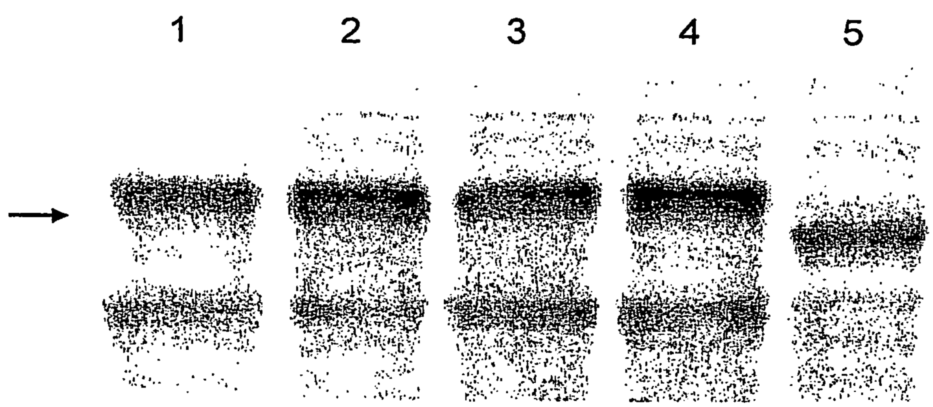

FIG.4

ELISA ASSAY

L1 CONSTRUCT	ng VLP/mcg TOTAL PROTEIN	FOLD INCREASE OVER WILD-TYPE
45 L1 WILD-TYPE	5 ng VLP/mcg TOTAL PROTEIN	na
45 L1 ISOLATE #4	12 ng VLP/mcg TOTAL PROTEIN	2.4
45 L1 R ISOLATE #11	10 ng VLP/mcg TOTAL PROTEIN	2.0

FIG.5

TRANSMISSION EM OF VLPs COMPOSED OF HPV 45 L1 R PROTEIN MOLECULES.

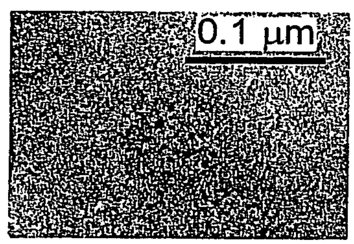

FIG.6